



## VALVULAR HEART DISEASE

### ELEVATED SEROTONIN LEVELS RESULTS IN ACCELERATED VALVE FIBROSIS IN STRETCH-OVERLOADED AORTIC VALVE

ACC Poster Contributions  
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**Background:** Aortic valve fibrosis has been reported in individuals with increased circulating serotonin/5-hydroxytryptamine (5HT) levels. In this study, we sought to understand the potential detrimental effects of elevated 5HT levels on stretch-overloaded aortic valve cusps.

**Methods:** Porcine aortic valve cusps were stretched in a tensile stretch bioreactor to 10% (physiologic) or 15% (pathologic) stretch in normal medium or medium supplemented with 5HT (10-6, 10-5, 10-4 M) as well as medium supplemented with serotonin receptor antagonists. Fresh valve cusps served as controls. Samples were analyzed for total collagen content, and expression of collagen I, III, lysyl oxidase, and hsp47. Samples were also tested for changes in tissue mechanical properties and tissue thickness.

**Results:** Collagen content ( $\mu\text{g}/\text{mg}$  tissue weight) in response to 10 $\mu\text{M}$  5HT was significantly higher ( $46.6 \pm 3.63$ ) than fresh controls ( $34.3 \pm 1.83$ ) and other concentrations of 5HT (10-6M:  $39.1 \pm 2.65$ ; 10-4M:  $24.0 \pm 1.01$ ). Lysyl oxidase, hsp47 and collagen I expression was highest for the 10-5M 5HT group compared to all other groups. Tissue thickness and stiffness was significantly increased for the 10-5M 5HT group.

**Conclusions:** The combined action of elevated stretch load and serotonin result in accelerated valve collagen synthesis and valve fibrosis. Culture with 5HT<sub>2A</sub> antagonists resulted in increased collagen content implying that other 5HT receptor subtypes regulate serotonin-related collagen turnover.